Effective Adaptive Immunity Relies on Lymph Node Remodeling

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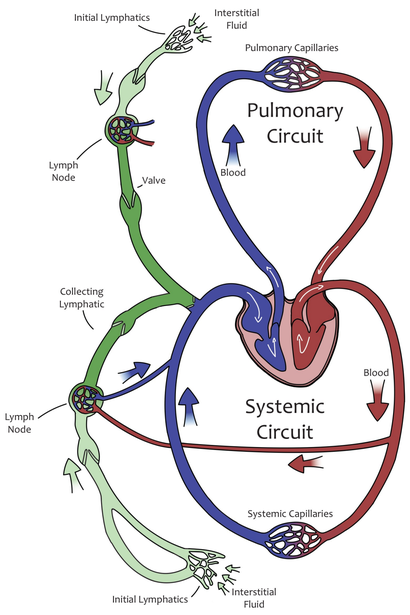
Background

Motivations

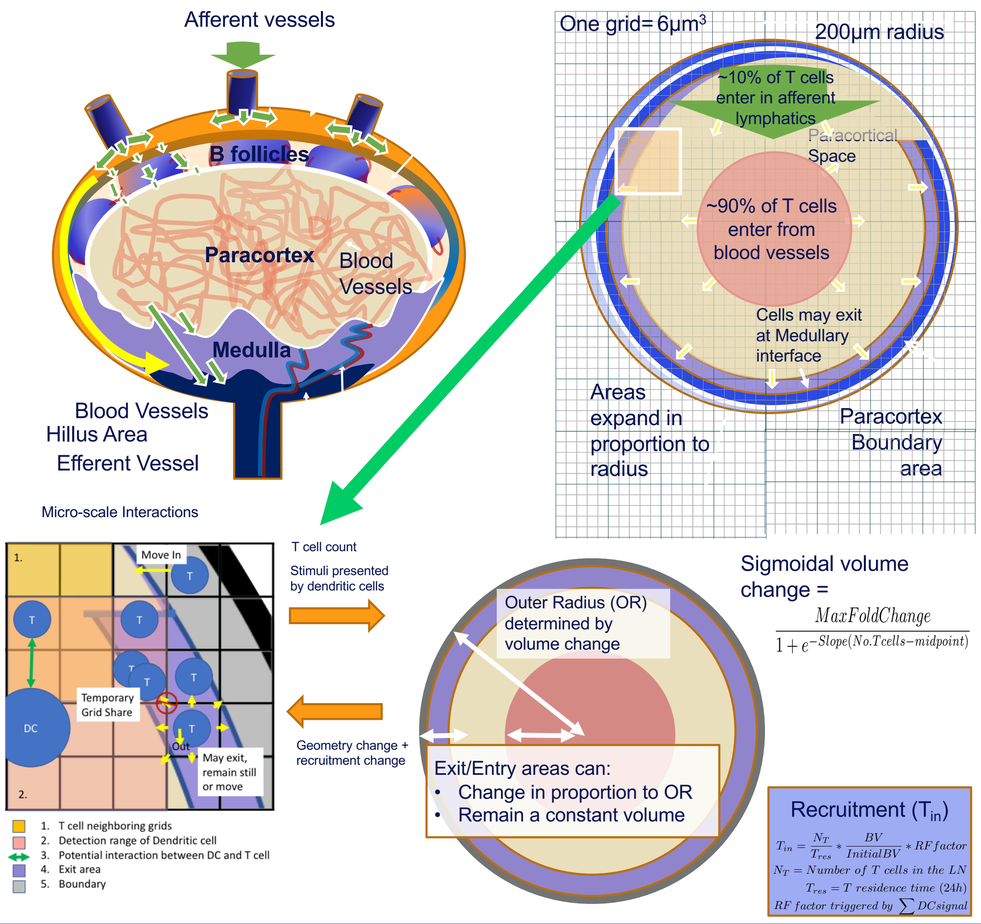
- All immune responses rely on lymph flow delivering antigen to lymph node
- Effective response requires appropriate T cell (TC) population distribution
- A well-developed model can improve our understanding of adaptive immunity



Goals of the Study

- Detailed information on temporal variations in TC subpopulations following antigen presentation
- Investigate the effects of lymph node volume expansion on production of TC subpopulations
- Couple the ABM with physical transport model of chemokine concentration gradients (in progress)

Agent-Based Model of Immune Cell Actions



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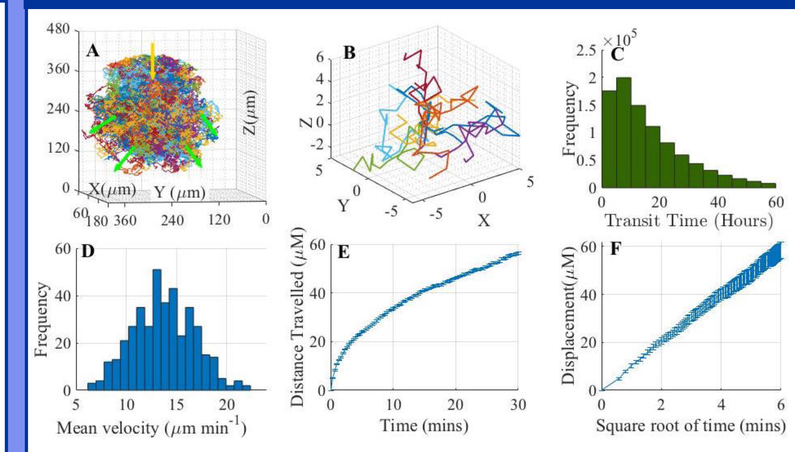
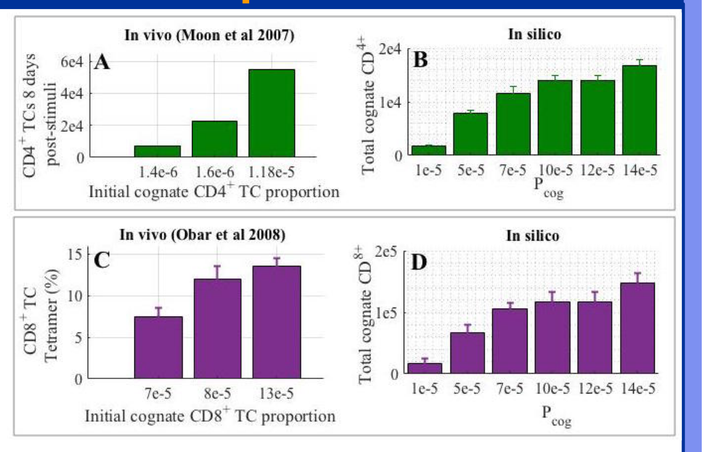
ABM Results I: Model Validation with Experiments

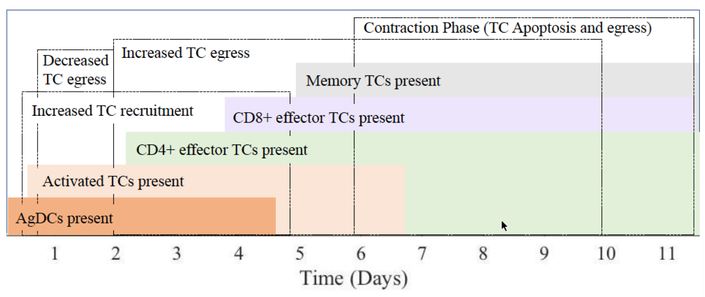


Modeling results representative of TC behaviors observed in vivo. A. TC tracking through the paracortex with individual tracks displayed. TCs entered centrally and in afferent lymph (yellow arrow). TCs exited at the periphery (green arrows). B. A selection of TC tracks (each color represents one TC path) transposed to the same origin point. C. TC transit time histogram. D. Mean TC velocity histogram. E. Mean and SEM (n=100) of TC displacement. F. Mean and SEM of TC displacement versus square root of time, indicating random walk behavior.

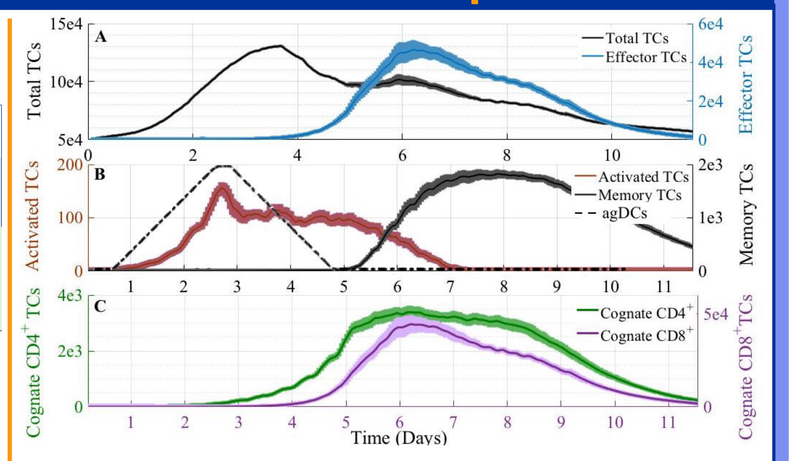


Comparison with TC responses observed experimentally. A. Variation in CD4+ response in mice to injected antigen as a function of initial proportion of cognate TCs (adapted from Moon et al., 2007). B. Equivalent modelling results, showing a trend of agreement. C. CD8+ response to 210e5PFU of either VSV-M45 or VSV-ova as a function of initial CD8+ proportion. (adapted from Obar et al., 2008). D. Equivalent modelling results, showing a trend of agreement.

ABM Results II: Baseline results with 20% volume expansion

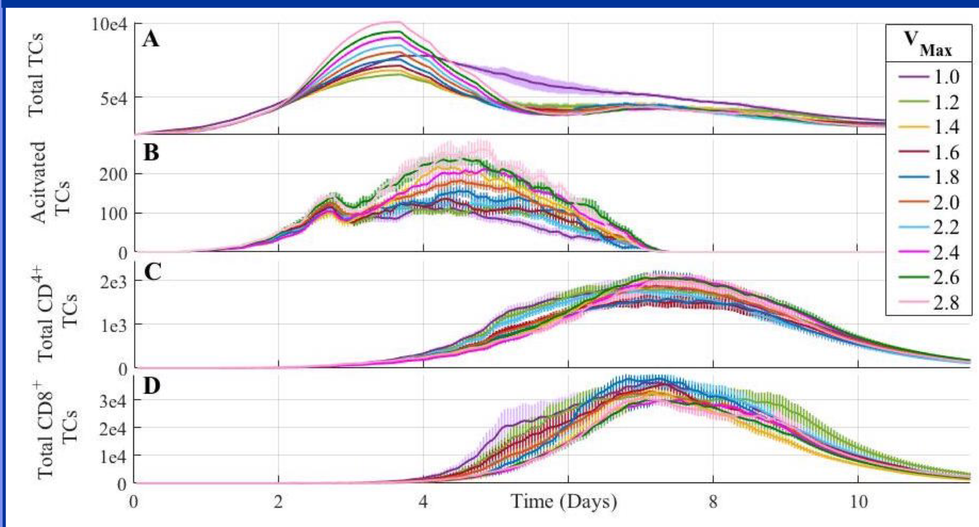


General time course of T cell trafficking and responses following antigen presentation.

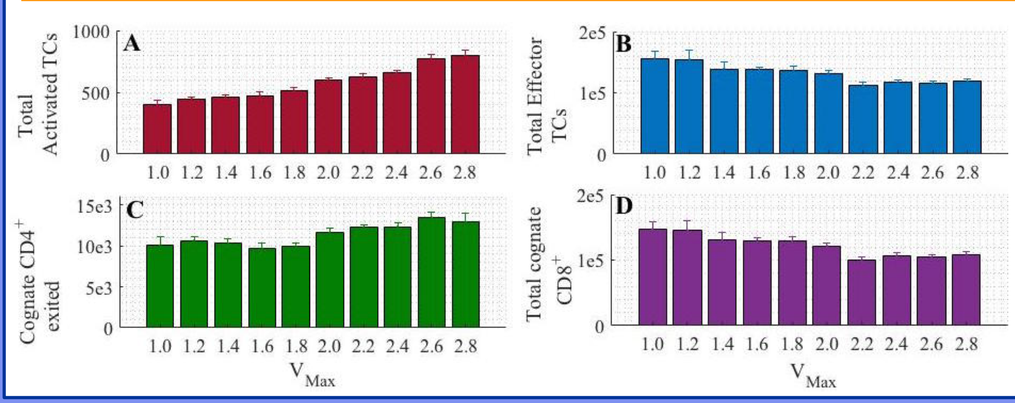


Types of TCs in the paracortex following entry of antigen-presenting Dendritic Cells (DCs, dot-dashed line in B). Average with SEM of 12 simulations.

ABM Results III: Effects of allowable volume expansion



The total TCs in the paracortex between day 2 and 5 increased with V_{Max}, except when the paracortex volume was fixed (V_{Max}=1). The number of activated TCs in the paracortex doubled when V_{Max} was increased from 1 to 2.8. The number of cognate CD4+ TCs in the paracortex showed no significant difference with V_{Max}.



Variations in total number of TC types produced as a function of VMax. Results from 7 simulations; average with SEM.